

### **REMARKS**

Claims 1-11 have been cancelled. Claims 12-18 have been withdrawn. Claims 19-24 have been added. There being no issue of new matter, entry of the foregoing amendments is respectfully requested.

#### **I. ELECTION**

During a telephone conversation with the Examiner applicant made a provisional election to prosecute the invention of Group I, claims 1-11 wherein a further election was made of a species of HCV protease having a first amino acid substitution at position 156 and at least a second substitution is the P89S substitution. Applicant hereby affirms this election is made **without** traverse. Applicant reserves the right to file on subject matter not selected here in divisional applications.

#### **II. CLAIM OBJECTIONS**

Applicant has cancelled the pending claims (1-11) and presents newly added claims 19-24 which are directed to the subject matter of elected Group I. The newly added claims incorporate the Examiners rejections and comments as further explained below.

The Examiner objected to claims 1-5 asserting that the claims fail to comply with 37 CFR §1.821 because they lack designation of a particular sequence. Newly added claims 19-24 have been drafted in order to overcome this ground for rejection and incorporate the appropriate sequence designation. Base claim 19 from which claim 20-24 are dependent recites an HCV protease comprising an amino acid sequence numbered according to SEQ ID No. 2 wherein the amino acid at position 156 is substituted with a non-alanine amino acid. Thus, these claims are in compliance with the requirements of 37 CFR §1.821. Applicant respectfully requests that this ground for rejection be withdrawn.

The Examiner objected to claims 1-5 and 9 for a number of informalities including repeated use of the preposition "at" and proper use of the indefinite article "an." Newly added claim 19-24

have been drafted in part to avoid these informalities.

The Examiner also suggested that the applicant amend claims 1-5 and 9 by substituting the term “modified” for “mutated.” While recognizing the Examiner’s comments applicant has amended the claims using the term “variant” rather than “modified” since the term “variant” is used in the applicant’s specification.

The Examiner also objected to the lack of a proper indefinite article “the” in the claims. Applicant has drafted the new claims to avoid this rejection.

*Claim rejection 35 USC §101*

The Examiner rejected claims 1-9 under 35 USC §101 on the assertion that they are not directed to statutory subject matter. Base claim 19 is directed to “variant HCV NS3 proteases. Also, the term “substitution” has been used in the claims rather than “mutation” as suggested by the Examiner.

*Claim rejections 35 USC §112*

The Examiner rejected claims 1-5 under 35 USC §112 first paragraph as containing subject matter not reasonably described in the specification. In particular, the Examiner asserts that the specification fails to exemplify the preparation of the proteases of claims 1-5 where the claims reach generic proteases that may differ at any or all amino acid positions of a protease. The Examiner further asserts that claims 1-5 fail to properly state a structural or functional requirement to distinguish the proteases. While applicant does not agree with the Examiner’s position, applicant has presented base claim 19 from which claim 20-24 are dependent. Claim 19 is directed to a variant HCV protease having serine protease activity and comprising an amino acid sequence numbered according to SEQ ID No. 2 wherein the amino acid at position 156 is substituted with a non-alanine amino acid. Thus, all of the instant claims are directed to HCV proteases having a particular structure.

The Examiner also asserts that the claims were not sufficiently enabled to allow one skilled in the art to practice the invention without undue experimentation. As noted above Applicant’s newly added claims clearly incorporate structural limitations defining the scope of the genus of

HCV protease of the invention. The specification discloses specific HCV proteases and in particular inhibitor resistant proteases having substitutions at amino acids 155, 156 or 168 of the native HCV protease sequence of SEQ ID No. 2.

The Examiner rejected claims 1 and 2 under 35 USC §112, second paragraph as being indefinite because claim 1 recites “comprised of an amino acid sequence in which the native HCV NS3 protease is mutated.” Applicant has accordingly, incorporating the structural limitation that the HCV variants be according to SEQ ID No. 2 in base claim 19.

*Claim rejections 35 USC §102*

The Examiner has rejected claims 1 and 5 under 35 USC §102(a) as being anticipated by Migliaccio et al. which discloses amino acids substitutions at positions D168A, D168Y, and D168V where position 168 corresponded to position 168 in SEQ ID No. 2. The Examiner also rejected claims 1-3 as being anticipated by Koch et al which discloses the amino acid substitution R155S, where position 155 corresponds to position 155 in SEQ ID No. 2. The Examiner also rejected claim 1 as being anticipated by Beyer et al. which discloses that the amino acid substitution D168Q and D168E. As noted above, applicant has directed the newly added claims to proteases according to SEQ ID No. 2 having substitutions at position 156. Thus, these grounds for rejection under 35 USC 102 should be withdrawn.

Applicant would also like to call to the attention of the Examiner WO 2005/042570 (US2005136400) which discloses NS3-NS4a protease resistant mutants. However, this reference has a priority date of April 13, 2004.

Authorization for payment of fees for a one month extension of time for reply to the Office Action is hereby given. It not believed that any other fees are required beyond those that may otherwise be provided for in accompanying documents. However, if additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. §1.136(a) and any fees required therefore are hereby authorized to be charged to our Deposit Account No. 02-2955.

If any points remain at issue which can best be resolved by way of a telephonic or personal

AMENDMENT  
US APPLN. NO. 11/034,281

interview, the Examiner is kindly requested to contact the undersigned attorney at the local telephone number listed below.

Respectfully submitted,

/David Dow/  
David Dow  
Reg. No. 46,124

Patent Department  
Boehringer Ingelheim Corp.  
900 Ridgebury Road  
P.O. Box 368  
Ridgefield, CT 06877  
Tel: (203) 791-6214  
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